

WHAT IS CLAIMED IS:

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5 1. A transgenic non-human animal having a mutated rchd534 gene, wherein said animal displays a cardiovascular disease symptom.

2. The animal of claim 1, wherein said cardiovascular disease symptom is hyperplasia, thickening of at least one cardiac valve, cardiac outflow tract development defects, cardiovascular calcification, epicardial vascular malformations, endocardial vascular malformation, or defects in the regulation of vascular tone.

10 3. The animal of claim 1, wherein said cardiovascular disease symptom is cardiovascular calcification.

15 4. The animal of claim 1, wherein said cardiovascular disease symptom is aortic or valvular calcification.

5. The animal of claim 1 which is a mouse.

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20 6. A cell having a mutated rchd534 gene isolated from the animal of claim 1, wherein said cell is isolated from tissue displaying a cardiovascular disease symptom.

25 7. The cell of claim 6, wherein said symptom is hyperplasia, thickening of at least one cardiac valve, cardiac outflow tract development defects, cardiovascular calcification, epicardial vascular malformation, endocardial vascular malformation, or defects in the regulation of vascular tone.

8. The cell of claim 6, wherein said symptom is cardiovascular calcification.

30 9. A cell line established from the cell of claim 6, wherein said cell is isolated from a tissue which exhibits at least one of the following cardiovascular developmental phenotypes: hyperplasia, thickening of at least one cardiac valve, cardiac outflow tract development defects, aortic ossification, epicardial vascular malformation, endocardial vascular malformation, or defects in the regulation of vascular tone.

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10. A method of producing a non-human animal having a mutated rchd534 gene, comprising introducing a polynucleotide into an embryonic cell of said animal through homologous recombination with an endogenous rchd534 gene, wherein said animal displays a cardiovascular disease symptom.

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11. The method of claim 10, wherein said cardiovascular disease symptom is hyperplasia, thickening of at least one cardiac valve, cardiac outflow tract development defects, cardiovascular calcification, epicardial vascular malformation, endocardial vascular malformation, or defects in the regulation of vascular tone.

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12. The method of claim 10, wherein said cardiovascular disease symptom is cardiovascular calcification.

13. The animal of claim 10, wherein said animal is a mouse.

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14. A method for diagnosing cardiovascular calcification, comprising assaying, in a patient sample, the level of an rchd534 gene product.

15. The method of claim 14, wherein the gene product comprises mRNA encoded by the nucleotide sequence set forth in FIGS. 6A-B or the nucleotide sequence set forth in FIGS. 10A-B.

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16. The method of claim 14, wherein the expression of a polynucleotide which hybridizes under highly stringent conditions to the nucleotide sequence set forth in FIGS. 6A-B or the nucleotide sequence set forth in FIGS. 10A-B is assayed.

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17. The method of claim 14, wherein the gene product comprises a polypeptide encoded by the nucleotide sequence set forth in FIGS. 6A-B or the nucleotide sequence set forth in FIGS. 10A-B.

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18. A method for diagnosing cardiovascular calcification, comprising determining, in a patient sample, the presence of a mutation in an rchd534 gene

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19. A method for diagnosing cardiovascular calcification, comprising determining, in a patient sample, the presence of a mutation in a gene containing the nucleotide sequence set forth in FIGS. 6A-B or the nucleotide sequence set forth in FIGS. 10A-B.
- 5 20. The method of claim 18 or 19 in which the mutation of the gene is assayed by:
- (a) obtaining a sample of cells from the patient;
 - (b) analyzing the structure of the gene in genomic DNA obtained from the sample of cells; and
 - (c) comparing the structure of the gene in the patient sample to the structure of the gene in a control sample of cells, in which a difference in the structure of the gene in the patient sample and the control indicates a mutation in the gene in the patient.
- 10 21. A method of monitoring the efficacy of a substance in clinical trials for the treatment or prevention of cardiovascular calcification, comprising assaying, in a patient sample, the expression of an rchd534 gene product.
- 15 22. The method of claim 21, wherein the gene product comprises mRNA encoded by the nucleotide sequence set forth in FIGS. 6A-B or the nucleotide sequence set forth in FIGS. 10A-B.
- 20 23. The method of claim 21, wherein the gene product comprises a polypeptide encoded by the nucleotide sequence set forth in FIGS. 6A-B or the nucleotide sequence set forth in FIGS. 10A-B.
- 25 24. A method for treating or preventing cardiovascular calcification, comprising administering a substance that modulates the expression of, or the activity of the encoded protein product of, the rchd534 gene.
- 30 25. A method for identifying a substance for treating or preventing cardiovascular calcification, comprising assaying the ability of the substance to modulate the expression of the rchd534 gene, or the activity of the rchd534 or rchd534-long protein product.
- 35 26. A method for identifying a substance for treating or preventing cardiovascular disease, comprising administering said substance to a non-human animal having a mutated

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rchd534 gene, wherein said animal displays a cardiovascular disease symptom, wherein amelioration of said cardiovascular disease symptom indicates a substance effective in the treatment or prevention of cardiovascular disease.

5 27. The method of claim 26, wherein said cardiovascular disease symptom is hyperplasia, thickening of at least one cardiac valve, cardiac outflow tract development defects, cardiovascular calcification, epicardial vascular malformation, endocardial vascular malformation, or defects in the regulation of vascular tone.

10 28. The method of claim 26, wherein said cardiovascular disease symptom is cardiovascular calcification.

15 29. A method of treating cardiovascular calcification in a mammal comprising administering to said mammal an amount of rchd534 agonist effective to reduce cardiovascular calcification in said mammal.

30 30. The method of claim 29, wherein said cardiovascular calcification is aortic or valvular calcification.

20 31. The method of claim 29, wherein said substance is a polynucleotide.

32. The method of claim 29, wherein said substance is a small organic molecule

25 33. The method of claim 29, wherein said substance is a polypeptide

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